PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.:

09/834,596

Confirmation No.: 4260

Applicant

Watanabe, et al. August 13, 2001

Filed TC/A.AU.

1623

Examiner

Howard V. Owens Jr.

Docket No.

08841.105037 PHAR 2020

Customer No.

20786

Title

2-' or 3'-Hydroxymethyl Substituted Nucleoside Derivatives for Treatment of

Hepatitis Virus Infections

Commissioner for Patents

P. O. Box 1450

Alexandria, VA 22313-1450

Transmittal of Supplemental Information Disclosure Statement

Sir:

The citation of information on the attached Form PTO-1449, "List of Art Cited by Applicant" is made pursuant to 37 C.F.R. §§ 1.56, 1.97, and 1.98. Copies of all listed references are enclosed. The citation of this information does not constitute an admission of priority or that any cited item is available as a reference, or a waiver of any right the applicant may have under applicable statutes, Rules of Practice in patent cases, or otherwise.

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Respectfully submitted,

Madeline I. Johnston

Reg. No. 36,174

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Complete if Known **Application Number** 09/834,596 Filing Date April 13, 2001 First Named Inventor Watanabe et al. **Group Art Unit** 1623 **Examiner Name** Howard V. Owens, Jr. **Attorney Docket Number** 08841.105037 PHAR 2020

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Examiner Initials *	Cite No. 1	Number Kind Codel		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages/Relevant Figures Appear
	AA	3,480,613		Walton et al.	11-25-1969	
	AB	5,977,061		Holy et al.	11-02-1999	
	AC	6,340,690	B1	Bachand et al. (Idenix Pharm.)	01-22-2002	
	AD	6,395,716	B1	Gosselin et al. (Idenix Pharm.)	05-28-2002	
	AE	6,444,652	B1	Gosselin et al.	09-03-2002	
	AF	6,573,248	B2	Ramasamy et al.	06-03-2003	
	AG	2002/0055483	A1	Watanabe et al.	05-09-2002	
	AH	2002/0147160	A1	Bhat et al.	10-10-2002	
	AI	2003/0008841	A1	Devos et al.	01-09-2003	
	AJ	2003/0028013	A1	Wang et al.	02-06-2003	
*******	. AK	2003/0050229	A1	Sommadossi et al. (Idenix Pharm.)	03-13-2003	
	AL	2003/0083307	A1	Devos et al.	05-01-2003	
	AM	2003/0087873	A1	Stuyver et al.	05-08-2003	

	FOREIGN PATENT DOCUMENTS								
Examiner Initials *	iner Cite			ment I Code ² known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶	
-	AN	FR	1,521,076		Merck & Co. Inc.	04-12-1968			
	AO	FR	1,581,628		Merck & Co. Inc.	09-19-1969			
	AP	FR	2,662,165 V	A1	Univ Pierre et Marie Curie, Paris	11-22-1991			
	AQ	GB	1,163,103 AV		Merck & Co. Inc.	09-04-1969			
	AR	GB	1,209,654 AV	Α	Merck & Co. Inc.	10-21-1970			
	AS	JP	63-215694 🗸	Α	Yamasa Shoyu Co. Ltd.	09-08-1988			
	AT	JР	06-228186 V	Α	Yamasa Shoyu Co. Ltd.	08-16-1994			
	AU	wo	98/16184 √/	A2	ICN Pharmaceuticals Inc.	04-23-1998			
	AV	wo	99/43691	A1	Emory U./Georgia Res. Found.	09-02-1999			

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First Named Inventor Watanabe et al.

Group Art Unit 1623

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	BA	wo	00/09531	A2	Novirio (Idenix Pharmaceuticals)	02-24-2000		T
	BB	wo	01/16671 ✓	A1	Novirio (Idenix Pharmaceuticals)	03-08-2001		Τ
	BC	wo	01/32153	A2	Biochem Pharma, Inc.	05-10-2001		T
	BD	wo	01/60315 J	A2	Biochem Pharma, Inc.	08-23-2001		Ι
	BE	wo	01/68663	• A1	ICN Pharmaceuticals Inc.	09-20-2001		
	BF	wo	01/79246 √,	A2	Pharmasset Ltd	10-25-2001		
	BG	wo	01/90121 🗸	A2	Novirio (Idenix); UnivCagliari	11-29-2001		
	BH	wo	01/91737 🏑	A2	Novirio (Idenix Pharmaceuticals)	12-06-2001		
	BI	wo	01/96353 🗸	A2	Novirio (Idenix); CNRC	12-20-2001		
	BJ	wo	02/03997	A1	ICN Pharmaceuticals Inc.	01-17-2002		
	BK	wo	02/18404 🗸	A2	F. Hoffmann-La Roche AG	03-07-2002		
	BL	wo	02/32920	A2	Pharmasset Ltd.	04-25-2002		
	BM	wo	02/48165 🗸	- A2	Pharmasset Ltd.	06-20-2002		
	BN	wo	02/057287 V	A2	Merck & Co. Inc.; Isis Pharm.	07-25-2002		
	ВО	wo	02/057425 🏑	A2	Merck & Co. Inc.; Isis Pharm.	07-25-2002		
·	BP	WO	02/070533 🗸	A2	Pharmasset Ltd.	09-12-2002		
	BQ	wo	02/094289 √	, A1	F. Hoffmann-La Roche AG	11-28-2002		
	BR	wo	02/100415 🗸	A2	F. Hoffmann-La Roche AG	12-19-2002		
	BS	WO	03/026589	A2	Novirio (Idenix Pharmaceuticals)	04-03-2003		\perp
	BT	wo	03/026675	A1	Novirio (Idenix Pharmaceuticals)	04-03-2003		\perp
	BU	WO	03/051899	A1	Ribapharm Inc.	06-26-2003		
·	BV	WO	03/061385	A1	Ribapharm Inc.	07-31-2003		
	BW	wo	03/061576	A2	Ribapharm Inc.	07-31-2003		
	BX	WO	03/062255	A2	Ribapharm Inc.	07-31-2003		\perp
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Attorney Docket Number

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	FOREIGN PATENT DOCUMENTS									
Examiner Initials *	Cite No. 1	Office ³	Foreign Patent Document Office ³ Number Kind Code ² (if known)		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶		
	CA	wo	03/063771	A2	Pharmasset Ltd.	08-07-2003				
	CB	wo	03/068162	A2	Pharmasset Ltd.	08-21-2003				
	CC	wo	03/072757	A2	Biota Inc.	09-04-2003		<u> </u>		
	CD	wo	03/093290	A2	Genelabs Technologies Inc.	11-13-2003				

		OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	CE	ALTMANN, K.H., et al., "The Synthesis of 1'-methyl carbocyclic thymidine and its effect on nucleic acid duplex stability", Synlett, Thieme Verlag, Stuttgart, De, October 1994, 10, 853-855	
	CF	BAGINSKY, S.G. et al., "Mechanism of action of a pestivirus antiviral compound," Proc. Nat. Acad. Sci. (USA) 2000, 97(14), 7981-7986.	
	CG	BEIGELMAN, L.N., et al, "Dimerization during the acetolysis of 3-O-acetyl-t-O-benzoyl-1,2-O-isopropylidene-3-C-methyl- α -D-ribofruanose. synethesis of 3'-C-methylnucleosides with the β -D-riboand α -D-arabino configurations", Carbohydrate Research, 1988, 181, 77-88.	
	СН	BEIGELMAN, L.N., et al, "A general method for synthesis of 3'-C-alkylnucleosides", Nucleic Acids Symp. Ser., 1981, 9, 116-119.	
	CI	BERENGUER et al, "Hepatitis B and C Viruses: Molecular Identification and Targeted Antiviral Therapies," Proceedings of the Association of American Physicians, 1998, 110(2), 98-112.	
·	CJ	CARROLL, S.S., et al. "Inhibition of Hepatitis C Virus RNA Replication by 2'-Modified Nucleoside Analogs," The Journal of Biological Chemistry, 2003, 278 (14), 11979-11984.	
	CK	CZERNECKI, S., et al, "Syntheses if Various 3'-Brached 2',3'-Unsaturated Pyrimidine Nucleosides as Potential Anti-HIV Agents," J. Org. Chem., 1992, 57, 7325-7328.	
	CL	DeFRANCESCO, R. et al., "Approaching a new era for hepatitis C virus therapy: inhibitors fot eh NS3-4A serine protease and the NS5B RNA-dependent RNA polymerase," Antiviral Research, 2003, 58, 1-16.	
	CM	FAIVRE-BUET, V., et al, "Synthesis of 1'-Deoxypsicofuranosyl-deoxynucleosides as Potential Anti-HIV Agents," Nucleosides & Nucleotides, 1992, 11(7), 1411-1424.	
	CN	FARKAS, J., et al., "Nucleic acid components and their analogues. XCIV. Synthesis of 6-amino-9-(1-deoxy-\(\sigma\)-D-psicofuranosyl)purine" Collect. Czech. Chem. Commun. 1967, 32, 2663-2667.	

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Sheet	4	of	7	Attorney Docket Number	08841.105037 PHAR 2020

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		OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	DA	FARKAS, J., "Nucleic acids components and their analogues. LXXIX. Synthesis of methyl 1-deoxy-D-psicofuranosides substituted at C(1) with haolo atoms or a mercapto group,", Collect. Czech. Chem. Commun. 1966, 31, 1535-1543.	
	DB	FEDEROV, I.I., et al, "3'-C-branched 2'-deoxy-5-methyluridines: Synthesis, enzyme inhibition, and antiviral properties,", J. Med. Chem., 1992, 35, 4567-4575.	
	DC	FRANCHETTI, P., et al, "2'-C-methyl analogues of selective adenosine receptor agonists: Synthesis and binding studies," J. Med. Chem., 1998, 41, 1708-1715.	
	DD	GROUILLER, A., et al., "Novel p-tolyenesulfonylation and thionocarbonylation of unprotected thymine nucleosides," Synlett, 1993, 221-222.	
	DE	HARAGUCHI, K., et al, "Preparation and reactions of 2'- and 3'- vinyl bromides of uracil-nucleosides: versatile synthons for anti-HIV agents," <i>Tetrahedron Letters</i> , 1991, 32(28), 3391-3394.	
	DF	HARRAGUCHI, K., et al, "Stereoselective synthesis of 1'-C-branched uracil nucleosides from uridine, Nucleosides & Nucleotides, 1995, 14, 417-420.	
	DG	HARRY-O'KURU, et al., "A short, flexible route toward 2'-C-branched ribonucleosides", J.Org. Chem. 1997, 62, 1754-1759	
	DH	HARRY-O'KURU, R.E., et al., "2'-C-Alkylribonucleosides: Design, Synthesis, and Conformation," Nucleosides & Nucleotides, 1997, 16 (7-9), 1457-1460.	
,	DI	HATTORI, H., et al., "Nucleosides and Nucleotides. 175. Structural requirements of the suga moiety for the antitumor activities of new nucleoside antimetabolites, 1-(3-C-ethynyl-β-D-ribopentofuranosyl)cytosine and -uracil," J. Med. Chem., 1998, 41, 2892-2902.	
	DJ	HREBABECKY, H. et al., "Nucleic acid components and their analogues. CXLIX. Synthesis of pyrimidine nucleosides derived from 1-deoxy-D-psicose," Collect. Czech. Chem. Commun. 1972, 37, 2059-2065	
	DK	HREBABECKY, H., et al., "Synthesis of 7- and 9β-D-psicofuranosylguanine and their 1'-deoxy derivatives," Collect. Czech. Chem. Commun. 1974, 39, 2115-2123	
	DL	IINO, T., et a.l, "Nucleosides and Nucleotides. 139. Stereoselective synthesis of (2'S)-2'-C-alkyl-2'-deoxyuridines," Nucleosides and Nucleotides, 1996, 15, 169-181.	
	DM	ITOH, Y., et al., "Divergent and stereocontrolled approach to the synthesis of uracil nucleosides branched at the anomeric position," J. Org. Chem., 1995, 60, 656-662.	
	DN	JOHNSON, C.R., et al, "3'-C-trifuloromethyl ribonucleosides, Nucleosides & Nucleotides, 1995, 14, 185-194.	

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	EA	KAWANA, M., et al, "The deoxygenation of tosylated adenosine derivatives with Grignard reagents," Nucleic Acids Symp. Ser., 1986, 17, 37-40.	
	EB	LAVAIRE, S., et al, "3'-deoxy-3'-trifluoromethyl nucleosides: synthesis and antiviral evaluation," Nucleosides & Nucleotides, 1998, 17, 2267-2280.	
	EC	LEYSSEN, P. et al., "Perspectives for the treatment of infections with Flaviviridae", Clinical Microbiology Reviews, Washington, D.C., (January 2000), 13(1), 67-82.	
	ED	MARTIN, X., et al., "Intramolecular hydrogen bonding in primary hydroxyl of thymine 1-(1-deoxy-β-D-psicofuranosyl) nucleoside," <i>Tetrahedron</i> , 1994, 50, 6689-6694.	
	EE	MATSUDA, A., et al., "Radical deoxygenation of <u>tert-alcohols</u> in 2-branched-chain sugar pyrimidine nucleosides: synthesis and antileukemic activity of 2'-deoxy-2'(<u>S</u>)-methylcytidine," <i>Chem. Pharm. Bull.</i> , 1987 , 35, 3967-3970.	
	EF	MATSUDA, A., et al., "Nucleosides and Nucleotides. 94. Radical deoxygenation of tert-alcohols in 1-(2-C-alkylpentofuranosyl)pyrimidines: Synthesis of (2'S)-2'-deoxy-2'-C-methylcytidine, an antileukemic nucleoside," J. Med. Chem., 1991, 34, 234-239.	
	EG	MATSUDA, A., et al, "Nucleosides and Nucleotides. 104. Radical and palladium-catalyzed deoxygenation of the allylic alcohol systems in the sugar moiety of pyrimidine nucleosides," <i>Nucleosides & Nucleotides</i> , 1992, 11(No. 2/4), 197-226.	
	EH	MATSUDA, A., et al., "Alkyl addition reaction of pyrimidine 2'-ketonucleosides: synthesis of 2'-branched-chain sugar pyrimidine nucleosides (Nucleosides and nucleotides. LXXXI.)," Chemical & Pharmaceutical Bulletin, March 1988, 36, 945-953.	
-	EI	MIKHAILOV, S.N., et al, "Synthesis and properties of 3'-C-methylnucleosides and their phosphoric esters," Carbohydrate Research, 1983, 124, 75-96.	
	EJ	MIKHAILOV, S.N., et al, "Hydrolysis of 2'- and 3'-C-methyluridine 2',3'-cyclid monophosphates and interconversion and dephosphorylation of the resulting 2'- and 3'-monophosphates: comparison with the reactions of uridine monophosphates," J. Org. Chem., 1992, 57, 4122-4126.	
	EK	MIKHAILOV, S.N., et al, "Substrate properties of C'-methylnucleoside and C'-methyl-2'-deoxynucleoside 5'-triphophates in RNA and DNA synthesis reactions catalysed by RNA and DNA polymerases," Nucleosides & Nucleotides, 1991, 10, 339-343.	
	EL	NUTT, R.F., et al., "Branched-chain sugar nucleosides. III. 3'-C-methyladenine," J.Org. Chem. 1968, 33, 1789-1795.	

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		OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS	
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	FA	OIVANEN, M., et al, "Additional evidence for the exceptional mechanism of the acid-catalysed hydrolysis of 4-oxopyrimidine nucleosides: hydrolysis of 1-(1-alkoxyalkyl)uracils. Seconucleosides. 3'-C-alkyl nucleosides and nucleosides 3',5'-cyclic monophosphates," J. Chem. Soc. Perkin Trans., 1994, 2, 309-314.	
	FB	ONG, S.P., et al, "Synthesis of 3'-C-methyl adenosine and 3'-C-methyluridine diphosphates and their interaction with the ribonucleoside diphosphate reductase from <i>Corynebacterium</i> nephridii," <i>Biochemistry</i> , 1992, 31, 11210-11215.	
	FC	PAN-ZHOU X-R, et al., "Differential effects of antiretroviral nucleoside analogs on mitochondrial function in HepG2 cells," Antimicrob Agents Chemother 2000; 44(no.3), 496-503.	
	FD	ROSENTHAL, A., et al, "Branched-chain sugar nucleosides. Synthesis of 3'-C-ethyl (and 3'-C-butyl)uridine," Carbohydrate Research, 1980, 79, 235-242.	
	FE	SAMANO, V., et al, "Nucleic acid related compounds. 77. 2',3'-didehydro-2',3'-dideosy-2'(and 3')-methylnucleosides via [3,3]-sigmatropic rearrangements of 2'(and 3')-methylene-3'(and 2')-O-thiocarbonyl derivatives and radical reducation of a 2'-chloro-3'-methylene analogue," Can. J. Chem., 1993, 71, 186-191.	
	FF	SAMANO, V., et al, "Synthesis and radical-induced ring-opening reactions of 2'-deoxyadenosine-2'-spirocyclopropane and its uridine analogs. Mechanistic probes for ribonucleotide reductases," J. Am. Chem. Soc., 1992, 114, 4007-4008.	
	FG	SCHMIT, C. et al., "The effects of 2'- and 3'-alkyl substituents on oligonucleotide hybridization and stability,", Biorganic & Medicinal Chemistry Letters, 1994, 4(No.16), 1969-1974.	
	FH	SERAFINOWSKI, P.J., et al, "New method for the preparation of some 2'- and 3'-trifluoromethyl-2'-3'- dideoxyuridine derivatives," <i>Tetrahedron</i> , 1999, 56(No. 2), 333-339.	
	FI	SHARMA, P.K., et al, "Synthesis of 3'-trifluoromethyl nucleosides as potential antiviral agents," Nucleosides, Nucleotides and Nucleic Acids, 2000, 19(No. 4), 757-774.	
	FJ	SOMMADOSSI J-P, et al., "Comparison of cytotoxicity of the (-)- and (+)-enantiomer of 2',3'-dideoxy-3'-thiacytidine in normal human bone marrow progenitor cells," Biochemical Pharmacology, 1992; 44:1921-1925.	
	FK	SOMMADOSSI J-P, et al., "Toxicity of 3'-azido-3'-deoxythymidine and 9-(1,3-dihydroxy-2-propoxymethyl)guanine for normal human hematopoietic progenitor cells in vitro," Antimicrobial Agents and Chemotherapy, 1987, 31(No. 3), 452-454.	
	FL	TRITSCH, D., et al., "3'-β-ethynyl and 2'-deoxy-3'-β-ethynyl adenosines: first 3'-β-branched-adenosines substrates of adenosine deaminase," Bioorganic & Medicinal Chemistry Letters, 2000, 10, 139-141.	

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Examiner Name	Howard V. Owens, Jr.
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<u> </u>	GA	TUNITSKAYA, V.L., et al, "Substrate properties of C'-methyl UTP derivatives in T7 RNA polymerase reactions. Evidence for N-type NTP conformation," FEBS Letters, 1997, 400, 263-266.	
	GB	USUI, H., et al, "Synthesis of 2'-deoxy-8,2'-ethanoadenosine and 3'-deoxy-8,3'-ethanoadenosine (Nucleosides and Nucleotides. LXIV)," Chem. Pharm. Bull., 1986, 34, 15-23.	
	GC	WALCZAK, K., et al, "Synthesis of 1-(3-alkyl-2,3-dideoxy-D-pentofuranosyl)uracils with potential anti-HIV activity," Acta Chemica Scand., 1991, 45, 930-934.	
	GD	WALTON, E., et al, "Branched-chain sugar nucleosides. V. Synthesis and antiviral properties of several branched-chain sugar nucleosides," J. Med. Chem., 1969, 12, 306-309.	
	GE	WOLFE, M.S., et al, "A concise synthesis of 2'-C-methylribonucleosides," Tetrahedron Letters, 1995, 36(No. 42), 7611-7614.	
	GF	WU, JC., et al, "A new stereospecific synthesis of [3.1.0] bicyclic cyclopropano analog of 2',3'-dideoxyuridine," <i>Tetrahedron</i> , 1990 , 46, 2587-2592.	
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